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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)

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Application Number	Filed
09/688,990	October 17, 2000
First Named Inventor	
Pierre CHARNEAU	
Art Unit	**Examiner**
1648	L.W.Z. Humphrey

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest.
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.

☒ attorney or agent of record.
Registration number 25,146.

☐ attorney or agent acting under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

Signature

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Typed or printed name

202-408-4033
Telephone number

May 29, 2008
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☒ *Total of 1 form(s) is/are submitted.

PRE-APPEAL BRIEF REVIEW

I. CLAIMS ON APPEAL

The claims on appeal are claims 41–46, 50, 51, and 66–73. Claims 62–65 and 74–77 were cancelled in an amendment under Rule 1.116 to simplify the issues for appeal.

II. APPELLANT'S INVENTION

Lentiviruses have the unique capacity among retroviruses of infecting differentiated non-mitotic cells. (Specification at p. 1, ll. 13–14.) The inventors searched the determinants involved in the entry of the retrovirus genome into infected cell nuclei, which is known as the nuclear import mechanism. (Id. at p. 1, ll. 23–24.) The discovery of the determinant essential for import led the inventors to design novel vectors for use in transferring genes, or more generally sequences of nucleotides termed "transgenes", into target cells. (Id. at p. 2, ll. 1–3.)

In particular, the inventors worked from HIV, a member of the lentivirus family, and identified and isolated a viral determinant responsible for the nuclear import of proviral DNA of HIV into target cells: Central triplex DNA. (Id. at p. 2, ll. 3–6)

Starting from the identification of the central triplex DNA as the essential nucleotide sequence for entry of the retrovirus into the nucleus of a target cell, the inventors produced a novel lentiviral vector, including the triplex DNA region. The introduction of this DNA fragment into a vector system increases transduction of genes into the cells by stimulating the amount of nuclear import of the vector DNA. (Id. at p. 3, ll. 21–25.)

All lentiviruses have *gag* and *pol* genes that encode Gag and Pol viral structural proteins. All lentiviruses also have cis-acting cPPT and CTS sequences. These cPPT and CTS sequences fall within *gag* and *pol* genes. (Compare Figs. 11F and 11E in the specification with GenBank Accession No. NC_001802 or AF033819.) Together, the cPPT and CTS sequences form the lentiviral central triplex DNA. (Id. at p.3, ll. 6–11.) The inventors discovered that this DNA triplex is able to function in vectors, out of the natural context of the lentiviral genome, as a nuclear import determinant enabling the vector genome to enter the nucleus of target cells. (Specification at p. 2, ll. 6–8.)

III. CLAIMS ON APPEAL

Appellant's claims are directed to a recombinant, non-replicative, non-infectious, lentiviral transfer vector containing the central triplex DNA. Three of the elements of the lentiviral triplex vector are:

1. a transgene to be transferred into the nucleus of a cell;

2. cPPT and CTS sequences for formation of the DNA triplex, which transfers the transgene into the nucleus of the cell; and

3. the absence of the functional *gag*, *pol*, and *env* genes from the lentiviral triplex vector.

(Amendment of Nov. 30, 2007, at p.5, claim 66.) The claims thus require a lentiviral DNA triplex that is out of its natural context in the lentiviral genome because "the vector is deprived of functional genes encoding lentiviral Gag, Pol, and Env proteins." (Specification at p. 2, ll. 6–8, and p. 8, ll. 1–4.)

IV. REJECTION UNDER 35 U.S.C. § 103(a)

The claims stand rejected under 35 U.S.C. § 103(a) as being obvious over Verma et al. ("Verma") taken in view of Charneau '94 and Charneau '92. (Office Action

of Feb. 26, 2008 at 3.) Appellant traverses the rejection because these references do not describe all of the elements of Appellant's claims or the relationship of these elements as claimed. The prior art does not describe, among other things, a lentiviral DNA triplex, out of its natural context of the lentiviral genome, for transfer of a transgene into the nucleus of a cell.

According to the Office, Verma discloses a recombinant, non-replicative, non-infectious retroviral transfer vector comprising: (1) a transgene encoding luciferase or β-galactosidase, and (2) retroviral regulatory signals, HIV-1 LTR, and RRE. Verma discloses two additional vectors, a packaging construct encoding HIV Gag, Pol, Vif, Tat, Rev and Nef, and a psuedotyping MLV vector encoding HIV Env. *See* Figure 1. (Office Action of Feb. 26, 2008 at 4.)

Verma's transfer vector does not contain cPPT and CTS sequences and thus cannot contain a lentiviral DNA triplex.

Only one of the other two vectors described by Verma could contain a lentiviral DNA triplex, namely, the "packaging construct." (*see* Verma at Fig. 1.) The "GAG" and "POL" genes in this packaging construct may contain the cPPT and CTS sequences necessary to form a DNA triplex, but the DNA triplex would not be out of its functional context of the lentiviral *gag* and *pol* genes. Indeed, a DNA triplex in Verma's construct would be part of the *gag* and *pol* genes, not "deprived" of them as required by the claims on appeal.

Further according to the Office, Charneau '94 discloses that the cPPT sequence is an important cis-acting sequence for initiating DNA transcription by priming DNA synthesis. The Office alleges that Charneau '94 further discloses a cis-acting HIV-1

CTS sequence that is essential for terminating DNA synthesis by displacing the completed DNA strand. According to the Office, Charneau '94 specifically discloses the nucleotide sequence of HIV-1 CTS. (Id.)

Apparently overlooked is the fact that the triplex DNA of Charneau '94 is in its functional context in the lentiviral genome, namely, the triplex DNA provides cis-acting sequences essential for viral replication. It is not out of its natural context. Charneau '94 does not disclose a lentiviral DNA triplex "deprived of functional genes encoding lentiviral Gag, Pol, and Env proteins" as required by the claims on appeal.

Finally, the Office cites Charneau '92 as disclosing the cPPT sequence. According to the Office, Charneau '92 also discloses that cPPT is an important sequence for initiating DNA transcription. (Id.)

The nucleotide sequence of the cPPT described in Charneau '92 is also in its functional location as a cis-acting element essential for replication of the viral genome. The cPPT sequence is not out of its natural context in the HIV-1 genome as required by the claims on appeal. It is not "deprived of functional genes encoding lentiviral Gag, Pol, and Env proteins."

And of course, since none of Verma, Charneau '94, or Charneau '92 describe a transfer vector containing the lentiviral DNA triplex and the transgene, none of them describes the functional requirement that "the DNA triplex transfers the defined nucleotide sequences into the nucleus of a cell" as recited in the claims. The function of a DNA triplex in its natural context in the lentiviral genes in Verma, Charneau '94, and Charneau '92 is to provide the cis-acting sequences essential for viral replication, as recognized by the Office. (Office Action of Feb. 26, 2008 at p. 4, citing to Charneau '94

and Charneau '92.) The function of the DNA triplex in Appellant's lentiviral triplex vector, however, is to transfer a transgene into the nucleus of a cell. This was unknown prior to Appellant's invention. The functional limitation that "the DNA triplex transfers the defined nucleotide sequences into the nucleus of a cell" cannot be disregarded. Indeed, it is impermissible to construe a claim to read out any limitation. *See K-2 Corp. v. Salomon S.A.*, 191 F.3d 1356, 1363, 52 U.S.P.Q.2d 1001, 1005 (Fed. Cir. 1999); *Ethicon Endo-Surgery, Inc. v. U.S. Surgical Corp.*, 93 F.3d 1572, 1578, 40 U.S.P.Q.2d 1019, 1023 (Fed. Cir. 1996).

V. CONCLUSION

It is the Examiner's burden to establish *prima facie* obviousness. *See In re Rijckaert*, 9 F.3d 1534, 1532, 28 U.S.P.Q.2d 1955 (Fed. Cir. 1993). Obviousness requires a suggestion of all the elements in a claim, *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1342, 68 U.S.P.Q.2d 1940 (Fed. Cir. 2003)), and "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1741, 82 U.S.P.Q.2d 1385 (2007). Here, the Examiner has not identified all the elements of Appellant's claims in Verma, Charneau '94, or Charneau '92, nor provided a reason that would have prompted the skilled worker to have arranged them in the manner necessary to reach the claimed invention. Accordingly, the rejection of Appellant's claims under 35 U.S.C. § 103(a) should be withdrawn.